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L16: Entry 15 of 15 File: USPT Feb 6, 1990

DOCUMENT-IDENTIFIER: US 4898932 A
TITLE: Monoclonal antibodies reactive with activated and oncogenic ras p21 proteins

Abstract Text (1):
Monoclonal antibodies reactive with oncogenic and activated ras p21 proteins containing glutamic acid, arginine or valine at position 12 and unreactive with normal ras p21 proteins containing glycine at position 12. The antibodies are secreted by hybridomas obtained by immunizing mice with synthetic dodecapeptides corresponding in amino acid sequence to positions 5-16 of normal ras p21 proteins, except having glutamic acid, arginine or valine in place of glycine at position 12. The antibodies and Fab fragments thereof are useful for diagnosis, staging and classification of malignant and premalignant lesions.

Application Filing Date (1):
19871022

Detailed Description Text (23):
Monoclonals antibodies E170, E184, R256 and DWP specifically react with activated ras proteins in malignant cells and do not react with ras proteins found in normal cells. Therefore, these monoclonal antibodies will be useful in the differentiation of normal and neoplastic cell in various immunological and biochemical assays. Secondly, these antibodies will permit the classification of neoplastic cells into various categories based on the particular ras protein expressed. These antibodies will be useful therefore in the quantitation of activated ras proteins which in turn will be useful in staging tumors based on levels of ras p21 expression. Thus, better diagnosis of malignant cells, the ability to differentiate malignant from premalignant cells and the ability to classfiy malignant cells into various categories due to levels of ras expression will result from the application of monoclonal antibodies E170, E184, R256 and DWP.

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L16: Entry 3 of 15 File: USPT Nov 13, 2001

DOCUMENT-IDENTIFIER: US 6316208 B1
** See image for Certificate of Correction **
TITLE: Methods for determining isolated p27 protein levels and uses thereof

Application Filing Date (1):
19970203

Detailed Description Text (84):
Detection of p27 stability may serve as a marker for the presence of cancerous cells and also allow for determination of the prognosis of the patient carrying the tumor. The subject method can be used to augment the detection and/or prognosis of such solid tumors as, for example, carcinomas (particularly epithelial-derived carcinomas) of such tissues as ovaries, lung, intestinal, pancreas, prostate, testis, liver, skin, stomach, renal, cervical, colorectal, and head and neck; melanomas; and sarcomas such as Kaposi's sarcoma and rhabdomyosarcoma. In preferred embodiments, the subject method is used to assess a malignant or pre-malignant epithelial carcinoma.

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L19: Entry 4 of 4 File: USPT Nov 16, 1999

DOCUMENT-IDENTIFIER: US 5984882 A
TITLE: Methods for prevention and treatment of cancer and other proliferative diseases with ultrasonic energy

Application Filing Date (1):
19971216

Detailed Description Text (19):
Overexpression of growth factors leads to suppression of cell death and has significant implications in the treatment of cancer. For example, the growth and proliferation of epithelial cells in prostate cancer is influenced by EGF, TGF-alpha, TGF-beta, NGF and FGF. The overexpression of these growth factors prevents DNA fragmentation and apoptotic mechanism (Chung, L. W. et al., 1992, J. Cell Biochem. Supplm. 16H:99-105). The methods of the present invention can induce apoptosis of growth factor receptor-bearing precancerous and cancerous cells and supporting stromal cells with ultrasonic energy.

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L19: Entry 1 of 4 File: USPT Oct 29, 2002

DOCUMENT-IDENTIFIER: US 6472376 B2
** See image for Certificate of Correction **
TITLE: Suppression of malignancy utilizing ribonucleotide reductase R1

Application Filing Date (1):
19980924

Brief Summary Text (8):
Regulation of ribonucleotide reductase, and particularly the R2 component, is markedly altered in malignant cells exposed to tumor promoters or to the growth factor TGF-.beta. [Amara, et al., 1994; Chen et al., 1993; Amara et al., 1995b; Hurta and Wright, 1995; Hurta et al., 1991]. An R1 deletion can be detected in some human colorectal carcinomas [Glenney, 1986]. Higher levels of enzyme activity have been observed in cultured malignant cells when compared to nonmalignant cells [Weber, 1983; Takeda and Weber, 1981; Wright et al., 1989a], and increased levels of R2 protein and R2 mRNA have been found in pre-malignant and malignant tissues as compared to normal control tissue samples [Saeki et al., 1995; Jensen et al., 1994]. Regulation of ribonucleotide reductase, and in particular the R2 component, is significantly elevated in transformed cells exposed to tumor promoters, or to transforming growth factor .beta. in growth factor mediated mechanisms of tumor progression [Amara et al., 1996; Chen et al., 1993; Amara et al, 1995b].

Detailed Description Text (64):
References Amara et al., 1994. Phorbol ester modulation of a novel cytoplasmic protein binding activity at the 3'-untranslated region of mammalian ribonucleotide reductase R2 mRNA and role in message stability. J. Biol. Chem. 269:6709-7071. Amara et al., 1995A. Altered regulation of message stability and tumor promoter-responsive cis-trans interactions of ribonucleotide reductase R1 and R2 messenger RNAs in hydroxyurea-resistant cells. Cancer Res. 55:4503-4506. Amara et al., 1995B. Defining a novel cis element in the 3'-untranslated region of mammalian ribonucleotide reductase component R2 mRNA: Role in transforming growth factor-.beta..sub.1 induced mRNA stabilization. Nucleic Acids Res. 23:1461-1467. Amara et al. 1996. Defining a novel cis-element in the 3'-untranslated region of mammalian ribonucleotide reductase component R2 mRNA: cis-trans interactions and message stability. J. Biol. Chem. 271:20126-20131. Ashihara and Baserga, 1979. Cell Synchronization. Methods Enzymol. 58:248-262. Betz et al., 1994, Basic Neurochem. Molecular Cell, (Raven Press Ltd, New York) 5th Ed., 681-699 Bickel, et al., 1993, "Pharmacologic effects in vivo in brain by vector-mediated peptide drug delivery" Proc. Natl. Acad. Sci. USA 90(7)2618-2622 Blaesse, 1997. Gene Therapy for Cancer. Scientific American 276(6):111-115. Bjorklund, et al., 1990. Biochemistry, 29:5452-5458 Bjorklund et al., 1993. Structure and promoter characterization of the gene encoding the large subunit (R1 Protein) of mouse ribonucleotide reductase. Proc. Natl. Acad. Sci. USA 90:11322-11326. Brem et al., "Polymers as controlled drug delivery devised for the treatment of malignant brain tumors" Eur. J. Pharm. Biopharm 39:2-7 (1993) Capecchi, "Altering the genome by homologous recombination" Science 244:1288-1292 (1989). Caras, et al 1985. Cloned Mouse Ribonucleotide Reductase Subunit M1 cDNA Reveals Amino Acid Sequence Homology with Escherichia coli and Herpesvirus Ribonucleotide Reductases. Biol Chem. 260:7015-7022. Chan et al., 1993. Phosphorylation of ribonucleotide reductase R2 protein: in vivo and in vitro evidence of a role for p.delta.4.sup.cdc2 and CDK2 protein kinases. Biochemistry 32:12835-12840. Chen et al., 1993. Mammalian ribonucleotide reductase R1 mRNA stability under normal and phorbol ester stimulating conditions: involvement of a cis-trans interaction at the 3'-untranslated region. EMBO J., 12:3977-3986. Chen et al., 1994A. Regulation of mammalian ribonucleotide reductase R1 mRNA stability is mediated by a ribonucleotide reductase R1 mRNA 3'-untranslated region cis-trans interaction through a protein kinase C-controlled pathway. Biochem. J. 302:125-132.

Chen et al., 1994B. Defining a novel ribonucleotide reductase R1 mRNA cis element that binds to an unique cytoplasmic trans-acting protein. Nucleic Acids Res., 22:4796-4797. Choy et al., 1988. Molecular mechanisms of drug resistance involving ribonucleotide reductase: hydroxyurea resistance in a series of clonally related mouse cell lines selected in the presence of increasing drug concentrations. Cancer Res. 48:2029-2035. Culver, 1998. Site-Directed recombination for repair of mutations in the human ADA gene. (Abstract) Antisense DNA & RNA based therapeutics, February, 1998, Coronado, Calif. Davis et al., 1994. Purification, Characterization, and Localization of Subunit Interaction Area of Recombinant Mouse Ribonucleotide Reductase R1 Subunit. Biol. Chem. 269:23171-23176. Egan, et al., 1987A. Expression of H-ras Correlates with Metastatic Potential: Evidence for Direct Regulation of the Metastatic Phenotype in 10T1/2 and NIH 3T3 Cells. Mol. Cell. Biol. 7:830-837. Egan et al., 1987B. 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